

Applicant : Leonard Guarente et al.  
Serial No. : 09/461,580  
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Attorney's Docket No.: 13407-016001 / MIT 8503

REMARKS

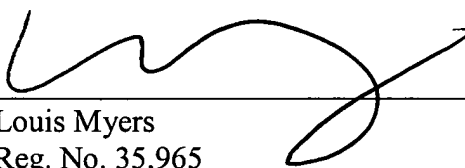
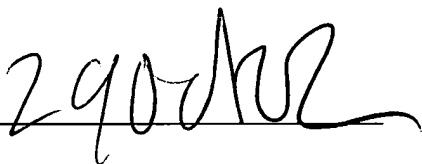
Applicants hereby submit that the enclosures fulfill the requirements under 37 C.F.R. §1.821-1.825. The amendments merely insert sequence identifiers in the specification and replace the original Sequence Listing with an amended substitute Sequence Listing. The substitute Sequence Listing contains the amino acid sequence "GAG(V/I)S(T/V)S (L/C/A)GIPDFRS" disclosed at page 42 of the specification, now SEQ ID NO:38. No new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment.

Please apply any charges or credits to Deposit Account No. 06-1050, referencing attorney docket number 13407-016001.

Respectfully submitted,

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**“Version With Markings to Show Changes Made”**

In the specification:

Paragraph beginning at page 38, line 17, has been amended as follows:

The term “core domain” (also referred to herein as “core”) refers to the evolutionarily conserved domains [fo] of Sir2 or Sir2-like proteins which can be identified, for example, by the comparison of amino acid sequences by, for example, CLUSTAL X, BLAST, PSI-BLAST or FASTA algorithms. The “core domain” is the domain that shows significant identity and/or homology to about 240-270 amino acids of Sir2 or Sir2-like proteins (about 20-50% or higher as amino acid identity, see Figure 2) and/or possesses the consensus sequence GAG(V/I)S(T/V)S(L/C/A)GIPDFRS (SEQ ID NO:[27] 38) and YTQNID (SEQ ID NO: 28) (Brachmann, *et al.*, *Genes & Development* 9:2888-2902, (1995)). The “core domain” of Sir2 proteins has NAD-dependent deacetylation and/or mono-ADP-ribosylation activities. Any protein with a “core domain” of a Sir2 protein, a fragment of the core domain, or any functional or structural equivalent which is capable of NAD-dependent deacetylation and/or mono-ADP-ribosylation of nuclear proteins is within the scope of the invention.